

Multiple categories of polycyclic aromatic hydrocarbons in atmospheric PM_{2.5} associated with changes in lipid profiles: a longitudinal study in Beijing

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Research

Keywords: polycyclic aromatic hydrocarbons (PAH), PM_{2.5} components, lipid profiles, biomarkers, repeated measurements

Posted Date: May 17th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-516053/v1>

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Version of Record: A version of this preprint was published at Atmospheric Environment on February 1st, 2022. See the published version at <https://doi.org/10.1016/j.atmosenv.2022.119005>.

Abstract

Background

Lipid disorder has been demonstrated as important biomarkers for many chronic diseases, while PM_{2.5} is becoming an emerging risk factor to altered lipid profiles. However, few studies have paid attention to the changes of comprehensive lipid indices caused by PM_{2.5}-bound polycyclic aromatic hydrocarbons (PAHs) exposure, especially among older adults population. We aimed to investigate whether PM_{2.5}-bound PAHs were associated with the changes of lipid profiles, and whether this association could differ among multiple categories of PAHs.

Methods

A longitudinal study including 98 adults was conducted in Beijing, China, from November 2016 to January 2018. Multiple categories of PAHs were classified into low-molecular-weight PAHs (LMW-PAHs), high-molecular-weight PAHs (HMW-PAHs), carcinogenic PAHs (c-PAHs) and non-carcinogenic PAHs (nc-PAHs) based on their molecular weight and carcinogenicity potential. Linear mixed-effects models were used to explore the association between multiple categories of PAHs and lipid profiles, including single-pollutant model, two-pollutant model, and constituent-residual model.

Results

We found that high-density lipoprotein cholesterol (HDL-C) levels were significantly decreased by 1.00% (95%CI, -1.98 to -0.30%) to 9.52% (95%CI, -13.93 to -4.88%) in association with a 10 ng/m³ increase in moving averages of the multiple categories of PAHs. We also found significant increases in total cholesterol (TG), castelli risk indexes I and II (CRI-I and II), and atherogenic coefficient (AC) by 4.08% (95% CI, 0.10 to 7.25%) to 40.49% (95% CI, 13.88 to 73.33%) were associated with a 10 ng/m³ increase of multiple categories of PAHs.

Conclusion

Multiple categories of PAHs were significantly associated with altered lipid profiles. Although some PAHs are not carcinogenic, they may cause dyslipidemia, which in turn affects chronic diseases.

Background

Lipid profiles are pre-clinical indicators that have been regarded as important predictive biomarkers for many chronic diseases, such as cardiovascular diseases (CVDs) and stroke [1–4], peripheral artery disease [5], type 2 diabetes mellitus [6], fatty liver [7], rheumatoid arthritis [8], and Alzheimer's disease [9].

Significantly, abnormalities in lipid profiles have a particularly profound influence on CVDs and represent around half of the population-attributable risk [10]. In fact, management of serum lipid levels has become a central objective in the effort to prevent cardiovascular events and the main target of therapy [11]. Although several traditional factors, such as age, sex, smoking [12] as well as alcohol consumption [13], have been closely related with alterations in blood lipid levels, recent studies suggested that new factors such as ambient air pollutants, especially particulate matter in aerodynamic diameter less than 2.5 μm ($\text{PM}_{2.5}$), were associated with altered lipid profiles [14–16]. Therefore, finding the key components of $\text{PM}_{2.5}$ that affect lipid levels is an urgent problem demanding prompt solution.

Polycyclic aromatic hydrocarbons (PAHs), composed of two or more fused aromatic (benzene) rings, have been considered as important components of primary organic aerosols [17]. Incomplete combustion of organic materials produces a large amount of PAHs, which diffuse through atmospheric transport, whereas PAHs are considered ubiquitous contaminants, detected in numerous environmental matrices such as air, fresh and groundwater, soil and sediments. [17]. PAHs have attracted worldwide attention because of their carcinogenicity and mutagenicity [18, 19]. Environmental epidemiological studies have utilized carcinogenic PAHs as the basis of molecular epidemiological research among residents exposed to ambient air pollutants [20]. Several investigations have revealed that PAHs exposure may increase the risk of chronic non-infectious diseases such as artery diseases as well as CVDs [21, 22], and oxidative stress may be one of the potential mechanisms [23, 24]. However, there has been a lack of research on ambient PAHs exposure and lipid profiles at population level.

Recent research showed that airway exposure to benzo(a)pyrene, mostly emitted from fossil fuel, wood and coal combustion [25], may dysregulate lipid metabolism of mice [26]. The underlying mechanism may be that PAHs activate aryl hydrocarbon receptor (AhR) signaling pathway, thereby mediating the abnormal expression of cytochrome P450 and promoting the development and progression of dyslipidemia [26, 27]. To our knowledge, there is a lack of studies comprehensively evaluating the effects of multiple categories of atmospheric PAHs on lipid profiles among general populations. This is essential for understanding the mechanism by which PAHs increase the risk of chronic non-infectious diseases. Therefore, in this prospective follow-up study we focused on the lipidemic effects following exposure to $\text{PM}_{2.5}$ -bound PAHs, with repeated measurements conducted from 2016 to 2018.

Methods

Study Participants and Design

From November 2016 to January 2018, we conducted a longitudinal study in order to investigate the health impacts of air pollution and its various chemical constituents on adults in Beijing. Based on the spatial distribution of the annual average $\text{PM}_{2.5}$ levels in 2015, five communities were selected as sampling sites to represent different pollutant levels in Beijing. Two samplers were set up at each sampling site [28]. We included participants who have lived in those communities for more than five years and will still be there in the next few years. Those who were unable to accomplish the follow-up

studies were excluded. Participants who had severe cardiovascular diseases (stroke, congestive heart failure and myocardial infarction) and cancers were also excluded. Four repeated measurements were conducted. Visit 1 was conducted from November 2016 to December 2016, then followed by 3 follow-ups: visit 2 in May 2017, visit 3 in November 2017, and visit 4 in January 2018. Health assessment questionnaires, physical examination and biological sample collection were performed during each visit. We included 98 participants who met the prespecified criteria. Among them, 97 completed all 4 visits, and 1 participant completed 3 visits. Thus, data from a total of 391 person-times was compiled and applied in this analysis. The ethics was approved by Institutional Review Board of Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences (IBMS, CAMS). Each participant completed a written informed consent.

Ambient PM_{2.5} sampling in the communities

During the field survey, we measured concentrations of PM_{2.5}, the US Environmental Protection Agency's (USEPA) 16 priority PAHs, organic carbon (OC) and element carbon (EC) at fixed samplers in each community. A total of ten fixed samplers were set up in five communities, including Fangshan, Dongcheng, Chaoyang, Liu Hegou and Qian Nantai, with no major roads or factories within a radius of 400, 150, 150, 150 and 160 meters, respectively. Medium flow samplers (TH-150C, Wuhan Tianhong, China) were used to measure PM_{2.5} mass concentration. Each sampler was equipped with quartz-fiber filters to determine the inorganic and organic constituents. Five daily successive samples were obtained prior to each visit.

Laboratory analysis for PAHs and other constituents

The PM_{2.5} mass concentrations were determined following the standard operation procedures. Further details can be found elsewhere [28]. Quartz filters were analyzed by a thermal-optical carbon analyzer (Model 2001A, Atmoslytic Inc., USA) to determine organic (OC) and elemental carbon (EC) [28].

In order to measure PAHs concentration, 1/2 of each filter was used for analysis. NAP-D₈, ACP-D₁₀, PHE-D₁₀, CHR-D₁₂ and BghiP-D₁₂ (AccuStandard Inc.) were used as recovery rate indicator. The samples of filter aliquots were extracted by ultrasonication for 60 min, with 90 ml of dichloromethane and acetone (1:1) solvent mixture. The solvent extracts were concentrated under reduced pressure on a rotary evaporator. The solvent was replaced by adding 10 ml *n*-hexane and continuing the rotary evaporation. Purification was performed using an aluminum peroxide/silica gel (1:2) column. PAHs were extracted with 70 ml dichloromethane/hexane (3:7) solvent mixture. The extract was rotary evaporated to 1 ml and then blown with nitrogen until dryness. Internal standards (m-terphenyl-d₁₄) was added prior to Gas chromatography-mass spectrometry (GC-MS) analysis (Agilent 7890A GC system, USA). Selected Ion Monitoring (SIM) was employed to quantify the 16 PAHs designated as high priority pollutants by the USEPA (naphthalene (NAP), acenaphthylene (ACY), acenaphthene (ACP), fluorene (FLU), phenanthrene (PHE), anthracene (ANT), fluoranthene (FLT), pyrene (PYR), benzo(a)anthracene (BaA), chrysene (CHR), dibenz(a,h)anthracene (DahA), benzo(b)fluoranthene (BbF), benzo(k)fluoranthene (BkF), benzo(a)pyrene

(BaP), indeno(1,2,3-cd)pyrene (IcdP) and benzo(g,h,i)perylene (BghiP)) [29]. The chromatographic condition was as follows: DB-5MS capillary column (60m×250µm×0.25µm) was used. The inlet temperature was 280 °C. Helium was used as the carrier gas with a flow rate of 1.5 mL/min. Split-flow sample injection was used with a split ratio was 4.5:1.

Given the cumulative lag effects of air pollutants [30], 1- to 5-days moving average (MA) concentrations of PAHs and other pollutants were examined. Specifically, 1-day MA was defined as the pollutant concentrations from 8 a.m. the day before clinic visit to 8 a.m. the day of the clinic visit, and 2-days MA was defined as the average pollutant concentrations from 8 a.m. two days before clinic visit to the day of clinic visit, etc.

Quality control and quality assurance

Recoveries were calculated by adding known concentrations of recovery indicators to each sample, where NAP-D₈ was the recovery indicator for NAP; ACP-D₁₀ as the recovery indicator for ACY, ACP, and FLU; PHE-D₁₀ as the recovery indicator for PHE and ANT; CHR-D₁₂ as the recovery indicator for FLT, PYR, BaA, and CHR; BghiP-D₁₂ as the recovery indicator for BbF, BkF, BaP, DahA, IcdP and BghiP. Blank values were deducted from the experimental data and the actual concentrations were recovery-corrected. The method limit of detection ranged from 0.4 to 0.9 ng/m³ and the instrument detection limit ranged from 0.05 to 0.94 µg/L. The concentration of PAHs below the detection limits was calculated as 1/2 of the detection limits. The average recoveries for each indicator ranged from 63.4% to 91.4%.

PAHs grouping

The sixteen PAHs measured in the current study were divided into four categories according to their molecular weight or carcinogenicity: (1) low-molecular-weight PAHs (LMW-PAHs), including those with less than four rings, i.e., NAP, ACY, ACP, FLU, PHE and ANT; (2) high-molecular-weight PAHs (HMW-PAHs), including those with four or more rings [17]; (3) carcinogenic PAHs (c-PAHs), including BaA, CHR, BbF, BkF, BaP, IcdP, DahA and BghiP; (4) non-carcinogenic (nc-PAHs), including the remaining eight PAHs [29, 31, 32]. SPAHs represents the total concentration of 16 PAHs.

Meteorological measurements

We obtained hourly temperature and relative humidity from the China Meteorological Administration for the entire study period. Daily averages of those meteorological parameters were calculated. 5-days moving average of temperature and relative humidity were calculated for further analysis.

Questionnaire, physical examinations and biomarker measurements

Our study used a standardized field survey protocol, with a brief description as follows: Standardized questionnaires were designed to collect the following information: age, sex, education levels, hypertension, diabetes, alcohol consumption, smoking, and indoor smoking status; Physical examination was carried out for each resident, including the measurement of sitting blood pressure, height and weight,

body mass index (BMI) was also estimated by the following equation: $\text{weight (kg)} \div \text{height}^2 \text{ (m}^2\text{)}$; Fasting venous blood of residents was collected at 8-9 a.m., and then blood glucose, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and triglycerides (TG) were measured in the Department of Clinical Laboratory within the Peking Union Medical College Hospital.

According to the information provided by questionnaire, physical examinations and biomarker measurements, we redefined diabetes and hypertension patients. Participants who reported physician-diagnosed diabetes or fasting blood glucose ≥ 7.0 mmol/L were defined as diabetes. Participants who reported physician-diagnosed hypertension or SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg were defined as hypertension.

Additionally, in order to comprehensively evaluate the changes in lipid profiles and their potential effects, several lipoprotein ratios or “atherogenic indices” were calculated [33], which better predict cardiovascular diseases than the isolated lipid parameters [34-36]. To be specific, the following equations were used:

1. Castelli risk indexes-I (CRI-I) = $\text{TC} / \text{HDL-C}$
2. Castelli risk indexes-II (CRI-II) = $\text{LDL-C} / \text{HDL-C}$
3. Non-HDL cholesterol (NHC) = $\text{TC} - \text{HDL-C}$
4. Atherogenic coefficient (AC) = $(\text{TC} - \text{HDL-C}) / \text{HDL-C}$

Statistical analysis

Ambient pollutants concentrations and population health data were merged according to the date of clinic visit. Hematological variables with heavily right-skewed distributions were log-transformed for further analyses. Spearman correlation coefficients between multiple categories of PAHs and the other pollutants were calculated.

Three linear mixed-effects models were fitted to evaluate the associations between multiple categories of PAHs and lipid profiles. In single-pollutant model (model 1), each category of PAHs with a specific days MA was incorporated as the fixed-effect term, and an unique identification (ID) for each participant was incorporated as the random-effect term. Several potential confounding factors were also included in this model: (1) individual characteristics, including age and BMI as continuous variables; sex, education, smoking and alcohol consumption as categorical variables; (2) meteorological factors were incorporated using natural splines with three degrees, including 5-days MA of mean temperature and relative humidity; (3) day of the week. We also fitted two-pollutant models (model 2) to control any potential confounding caused by other pollutants, each of which included adjustment for $\text{PM}_{2.5}$, OC, and EC on the same specific days MA with PAHs, respectively. In order to control the collinearity among different pollutants, constituent-residual models (model 3) were fitted. Residuals were obtained in a linear model containing both $\text{PM}_{2.5}$ and a specific category of PAHs and then added into the main model replacing pollutants.

We performed stratified analysis by cigarette smoking (yes, no), alcohol consumption, age (< 65y, ≥ 65y), BMI (< 25, ≥ 25), diabetes mellitus and hypertension. In addition, several sensitivity analyses were applied to test the robustness of the associations. (1) considering the potential associations between indoor smoking and indoor PAHs exposure [37], participants who were smokers or lived in smoker residency were excluded. (2) participants with diabetes or hypertension were excluded. (3) FLU was included in c-PAHs because of its relatively higher toxic equivalent factor compared to BghiP [38]. (4) the association between multiple categories of PAHs abundances per g of PM_{2.5} and lipid profiles were evaluated.

All statistical analyses were performed with R software, version 3.5.0 (R Foundation for Statistical Computing), using “lme4” and “splines” packages. For the association between PAHs concentrations and lipid profiles, model estimates were calculated as per 10 ng/m³ increase in PAHs exposure. For the association between PAHs abundances and lipid profiles, model estimates were calculated as per 1/1000 increase in PAHs abundances. A *p*-value less than 0.05 was considered statistically significant.

Results

Table 1 shows the demographic characteristics of 98 participants. Among them, 38 (38.8%) were male and 60 (61.2%) were female, with mean age of 62.7 ± 9.9 years, while 56 (57.1%) had a BMI of 25 kg/m² or more. Among them, 23 (23.5%) were current smokers, 24 (24.5%) were exposed to indoor smoking and 37 (37.8%) were regular drinkers, 34 (34.7%) had diabetes mellitus, and 65 (66.3%) had hypertension.

Table 1
Demographic characteristics of 98 participants.

Characteristic	Mean ± SD or n (%)
N	98
Sex	
Male	38 (38.8)
Female	60 (61.2)
Age (years)	62.7 ± 9.9
BMI (kg/m²)	
BMI < 25	42 (42.9)
BMI ≥ 25	56 (57.1)
Education level	
Below high school	55 (56.1)
High school and above	43 (43.9)
Cigarette smoking	
No	75 (76.5)
Yes	23 (23.5)
Indoor smoking	
No	74 (75.5)
Yes	24 (24.5)
Alcohol consumption	
No	61 (62.2)
Yes	37 (37.8)
Diabetes mellitus	
No	64 (65.3)
Yes	34 (34.7)
Hypertension	
No	33 (33.7)

Abbreviation: SD: standard deviation.

Characteristic	Mean ± SD or n (%)
Yes	65 (66.3)
Abbreviation: SD: standard deviation.	

Figure 1 depicts the distribution of 16 PAHs during each visit. In winter (visit 1, visit 3, and visit 4), HMW-PAHs, especially 4-rings PAHs (including CHR, FLT, PYR and BaA), were the main pollutants, followed by 5-ring PAHs such as BbF.

Table 2 shows substantial variabilities in the concentrations of ambient pollutants and meteorological measures across the study period. Median concentrations of Σ PAHs during the four visits were 50.9, 67.0, 11.9 and 68.7 ng/m³, respectively, while PM_{2.5} exhibited median concentrations of 118.7, 63.8, 117.8 and 70.9 μ g/m³, respectively. Table S1 shows the mean concentrations for 16 individual PAH. Table 3 summarizes lipid indices during each visit. HDL-C, CRI-I and AC levels were significantly different throughout a series of four measurements.

Table 2

Descriptive statistics of ambient air pollutants and meteorological measurements at each visit.

Variables	Visit 1	Visit 2	Visit 3	Visit 4	<i>p</i>
2-days moving average of ambient pollutants (median (IQR))					
ΣPAHs (ng/m ³)	50.9 (28.3, 76.8)	67.0 (54.9, 78.8)	11.9 (7.0, 17.1)	68.7 (40.8, 89.3)	< 0.001
LMW (ng/m ³)	3.9 (2.9, 7.7)	24.1 (18.9, 29.0)	3.2 (1.7, 4.4)	6.7 (4.1, 11.2)	< 0.001
HMW (ng/m ³)	46.2 (23.7, 70.8)	39.9 (28.3, 49.0)	9.3 (3.4, 12.9)	62.0 (34.9, 78.0)	< 0.001
nc-PAHs (ng/m ³)	16.4 (8.1, 30.7)	39.7 (30.3, 49.6)	4.0 (2.6, 6.1)	29.8 (13.3, 42.4)	< 0.001
c-PAHs (ng/m ³)	30.7 (16.4, 45.6)	27.6 (20.9, 31.0)	8.4 (3.1, 11.8)	37.2 (26.1, 50.2)	< 0.001
OC (μg/m ³)	17.8 (9.4, 39.4)	8.2 (6.8, 10.8)	8.0 (6.2, 9.9)	6.9 (5.3, 10.6)	< 0.001
EC (μg/m ³)	6.1 (2.5, 10.4)	3.4 (2.3, 4.4)	2.7 (1.4, 3.5)	2.0 (1.2, 2.6)	< 0.001
PM _{2.5} (μg/m ³)	118.7 (45.1, 240.8)	63.8 (57.7, 86.4)	117.8 (50.2, 156.4)	70.9 (54.1, 88.2)	0.018
5-days moving average of meteorological measurements (mean (SD))					
Humidity (%)	65.9 (9.2)	47.3 (4.5)	60.0 (2.0)	42.6 (10.9)	< 0.001
Temperature (°C)	2.8 (2.6)	26.4 (2.6)	6.7 (1.2)	-7.2 (0.0)	< 0.001
Abbreviation: PAHs: polycyclic aromatic hydrocarbons; LMW: low molecular weight; HMW: high molecular weight; nc-PAHs: non-carcinogenic PAHs; c-PAHs: carcinogenic PAHs; OC: organic carbon; EC: element carbon; PM _{2.5} : Particulate matter in aerodynamic diameter less than 2.5 μm.					

Table 3
Descriptive statistics of lipid profiles (mean (SD)) at each visit.

Lipid profiles	Visit 1	Visit 2	Visit 3	Visit 4	<i>p</i>
HDL-C	1.30 (0.26)	1.18 (0.25)	1.32 (0.29)	1.23 (0.27)	0.001
LDL-C	2.96 (0.86)	2.90 (0.75)	3.05 (0.86)	2.81 (0.80)	0.224
TC	4.93 (1.04)	4.78 (0.85)	4.83 (0.98)	4.62 (1.00)	0.152
TG	1.68 (1.28)	1.54 (1.17)	1.51 (0.92)	1.65 (1.05)	0.654
CRI-I	3.92 (1.03)	4.21 (1.08)	3.78 (0.91)	3.87 (0.95)	0.018
CRI-II	2.35 (0.73)	2.55 (0.78)	2.39 (0.75)	2.36 (0.76)	0.220
AC	2.92 (1.03)	3.21 (1.08)	2.78 (0.91)	2.87 (0.95)	0.018
NHC	3.63 (1.01)	3.60 (0.84)	3.51 (0.92)	3.39 (0.94)	0.259
Abbreviation: HDL-C: high-density lipoprotein cholesterol (mmol/L); LDL-C: low-density lipoprotein cholesterol (mmol/L); TC: total cholesterol (mmol/L); TG: triglycerides (mmol/L); CRI-I: Castelli risk indexes I; CRI-II: Castelli risk indexes II; AC: atherogenic coefficient; NHC: non-HDL cholesterol (mmol/L).					

There were weak correlations between Σ PAHs and OC, EC as well as $PM_{2.5}$, the correlation coefficients were 0.39, 0.34 and 0.29, respectively ($p < 0.05$ in all case; Table S2).

Figures 2 and 3 present the different days MA patterns of percentage change in eight lipid classes or indices associated with a 10 ng/m^3 increase in each category of PAHs. In model 1, HDL-C levels were reduced by 1.00% (95%CI, -1.98 to -0.30%) to 9.52% (95%CI, -13.93 to -4.88%) in association with a 10 ng/m^3 increase in exposure to all categories of PAHs from 1- to 5-days MA (Fig. 2). By contrast, the largest increases in TG levels by 4.08% (95%CI, 0.20 to 8.33%) to 17.35% (95%CI, 2.02 to 33.64%) were associated with a 10 ng/m^3 increase in LMW PAHs, nc-PAHs, or Σ PAHs from 2- to 5- days MA (Fig. 2). We also observed a marginally significant increase in TG levels by 6.18% (95%CI, -0.99 to 12.75%) to 8.33% (95%CI, -0.99 to 19.72) associated with a 10 ng/m^3 increase in c-PAHs from 2- to 5- days MA (Fig. 2).

For atherogenic indices, significant increases in CRI-I were observed in associations with a 10 ng/m^3 increase in multiple categories of PAHs at 2- to 5- days MA, ranging from 7.25% (95% CI, 2.02 to 13.88%) to 40.49% (95% CI, 13.88 to 73.33%) (Fig. 3). CRI-II was significantly increased by 4.08% (95% CI, 0.10 to 7.25%) to 16.18% (95% CI, 2.02 to 33.64%) in association with a 10 ng/m^3 increase in all categories of PAHs at 3- to 5- days MA (Fig. 3). Concomitantly, significant increases in AC were also observed in association with different categories of PAHs (Fig. 3). Our primary results remained robust in model 2 (Figure S1 to Figure S6) or model 3 (Figure S7 and Figure S8).

In subgroup analysis, elevated levels of LDL-C, TC, CRI-II and NHC were observed in smokers. Figure S9 shows the percentage changes in eight lipid indices stratified by smoking status. Among smokers, we

observed per 10 ng/m³ increase in c-PAHs associated with 37.71% (95% CI, 9.42 to 73.33%), 49.18% (95% CI, 12.75 to 97.39%), 36.34% (95% CI, 13.88 to 64.87%) and 47.69% (95% CI, 9.42 to 99.37%) increments in LDL-C, TC, CRI-II and NHC at prior 2-days MA, respectively. However, significant decrease in HDL-C, significant increase in TG, CRI-I and AC were observed in non-smokers. Similar results can be observed in subgroup analysis by alcohol consumption (Figure S10). Furthermore, we found multiple categories of PAHs were significantly associated with lipid indexes among participants \geq 65 years old, BMI \geq 25 kg/m², non-diabetes participants, and hypertension participants (Figure S11 to Figure S14).

Our primary results remained robust in sensitivity analysis among participants from non-smoker residences. HDL-C levels were reduced by 1.00% (95%CI, -2.96 to -0.30%) to 10.42% (95%CI, -15.63 to -4.88%) in association with a 10 ng/m³ increase in exposure to all categories of PAHs from 1- to 5-days MA (Fig. 4). TG was significantly increased by 6.18% (95% CI, 1.01 to 11.63%) to 33.64% (95% CI, 8.33 to 66.53%) in association with a 10 ng/m³ increase in LMW PAHs, nc-PAHs, and Σ PAHs (Fig. 4). We also observed significant increase in CRI-1 and AC associated with PAHs exposure from 2- to 5-days MA (Fig. 5). When participants with diabetes or hypertension were excluded, HDL-C levels were significantly associated with LMW-PAHs in 1-day MA. The associations of Σ PAHs and TG were enhanced, with an increase of TG levels by 5.13% (95% CI, 0.30 to 11.63%) to 9.42% (95% CI, 1.01 to 17.35%). However, the associations of multiple categories of PAHs and CRI-I and AC were attenuated with small and marginally significant associations ($p < 0.1$). CRI-I and AC increased ranging from 12.75% (95% CI, -0.10 to 28.40%) to 28.40% (95% CI, -0.30 to 66.53%) (Figure S15 and Figure S16). Additionally, reclassification of FLU resulted in no significant changes in the results (Figure S17 and Figure S18). Similarly, our main findings remained robust when assessing the association between PAHs abundances and lipid profiles (Figure S19).

Discussion

This longitudinal study was conducted mainly to investigate the associations between multiple categories of PAHs and lipid profile alterations. Our study shows that different categories of PAHs mixtures, including LMW (<4-rings), HMW (\geq 4-rings), carcinogenic and non-carcinogenic PAHs, could promote significant, but different patterns of alterations in blood lipids. We also found that PAHs may increase the level of blood lipid indices, such as the CRI-I and CRI-II, both of which are important indicators of vascular risk, and are more sensitive than the isolated lipid parameters. These findings provide epidemiological evidence that PM_{2.5}-associated PAHs might be a novel risk factor to CVDs, prompting that traditional risk factors cannot explain all of CVDs [39]. Our results also suggest that exposure to various PAHs, whether carcinogenic or not, might cause lipid disorders, thus increasing the risk of chronic diseases.

We explored the relationship between multi-categories of atmospheric PAHs and lipid profiles among general community populations for the first time. Considering that cigarette smoking is one of the main indoor PAHs sources, we also assessed this relationship in participants from non-smoker residences. Our

findings provide evidence that environmental PAHs may disturb proatherogenic lipid profiles, as evidenced by decreased HDL-C levels, increased TG levels, and increased atherosclerotic indices such as CRI-I, CRI-II and AC. This may further trigger several chronic diseases (e.g., CVDs) under a real-world exposure scenario. These findings extended our current knowledge on population-based health outcomes following exposure to PM_{2.5} constituents, which are novel and of great significance to public health.

Compositions of different PAHs can be used to indicate varying emission sources. In this study, we divided 16 priority PAHs into multiple categories based on their molecular weight and carcinogenicity. LMW-PAHs are considered to be less carcinogenic than HMW-PAHs [40, 41]. However, the former usually have a higher concentration in the urban and are more likely to produce toxic secondary pollutants. Coke production, wood and coal combustion and vehicular emissions are the main sources of LMW-PAHs, such as PHE and ANT [42]. HMW-PAHs exhibit nearly all the carcinogenic potential of total PAHs, which were considered to be the leading biologically active pollutants in the atmosphere [43]. Sources of HMW-PAHs include car exhausts (petrol and diesel), incinerators, wood combustion, oil burning, domestic coal-stove emissions and tobacco smoke [41, 42]. Our self-monitored pollutant data revealed that the concentrations of LMW-PAHs was highest in spring, with a higher LMW/HWM ratios, which means that petrochemical processes or fuel evaporation was the major sources of PAHs [42]. On the contrary, HMW-PAHs, especially 4-ring congeners, had the highest concentrations in winter, which might be due to increased emissions caused by heating, and reduced dispersion of pollutants caused by meteorological factors in cold environments [44]. The results of HMW-PAH concentrations are overall consistent with other reports in Beijing [42]. More importantly, the associations between PAHs exposure and lipid indices remained significant regardless of the molecular weight or the carcinogenicity. Our results provided environmental epidemiological evidence that PAHs exposure can lead to disruption of pre-clinical indicators, and even to increase the risk of chronic diseases such as CVDs. Therefore, atmospheric PAHs should be controlled either by source-directed measures like filtering pollution from relevant industries (e.g., incinerator) or limiting automobile emissions.

Although no studies have directly investigated the relationship between atmospheric PAHs and lipid profiles, some articles have explored the effect of urinary PAH metabolites on isolated lipid parameters. A cross-sectional Chinese study showed that exposure to 1-hydroxynaphthalene, 9-hydroxyfluorene, 1-hydroxyphenanthrene, 4-hydroxyphenanthrene, and 9-hydroxyphenanthrene may increase TC levels [45]. In addition, exposure to 1-hydroxynaphthalene may also increase LDL-C levels. However, these PAH metabolites may not change hyper-TG levels [45]. Ranjbar et al. reported that exposure to high levels of PAH metabolites were related to a greater likelihood of dyslipidemia in a dose-dependent manner [46]. However, a research from southern Sweden did not find significant association of urinary PAH metabolites on HDL-C or TC in chimney sweepers [47]. These inconsistent findings might be the result of differences in the demographic characteristics of the participants and PAH exposure sources. This may indicate that the effects of different PAH chemicals on lipid metabolism are heterogeneous.

The underlying mechanisms of PAH impact on lipid metabolism are not fully understood, but the activated aryl hydrocarbon receptor (AhR) signaling pathway may be involved in this process. Metabolic

profile of PAHs could accelerate by inducing microsomal cytochrome P450, which is mediated by binding to a cytosolic receptor protein, the AhR. Alexander et al. showed that the activation of AhR signaling pathway may promote TG accumulation and ultimately cause lipid metabolism disorders [48]. In addition, because of PAHs' distribution and metabolism characteristics, the highest extent of metabolism usually occurs in the liver, while adipose tissue contains higher PAHs concentrations compared with other tissues. As is well documented, apolipoprotein A and apolipoprotein B are synthesized in the liver and are the major structural component of HDL-C and LDL-C, respectively. It is not clear whether PAHs could directly affect apolipoprotein production in the liver or whether it could be distributed in adipose tissue to alter lipid deposition.

There are several advantages in this longitudinal study. First, this study has a relatively large sample size, along with repeated measurements. All participants lived in their community for more than five years and without occupational exposure to PAHs. Most of them were older and more sensitive to the harmful impacts of atmospheric PAHs. Second, the original sixteen priority PM_{2.5}-bound PAHs were detected in this study, which reflects the unique characteristics of particulate PAHs in the community's environment. Third, we used a comprehensive lipoprotein ratio or "atherogenic indices" instead of isolated lipid parameters, which optimized its predictive value for CVDs.

Several study limitations should also be noted. First, more sampling sites should be added to better reflect the distribution of PAHs in Beijing. Second, individual exposure assessment was based on the community levels, so that there was a lack of accuracy on the individual level, which could be advanced in further work. Third, indoor environments are also key factors in health risk assessment in residences. Indoor smoking, heating and incense burning are main sources of indoor PAHs [37]. In this study, indoor PAHs concentrations were not monitored given the limitation in equipment and human hands, which should be improved in further studies. However, in order to reduce the potential effects caused by indoor PAHs. We collected smoking status and indoor smoking and excluded potential smokers in sensitivity analysis. The results were almost consistent with our main findings. In addition, participants in this study used central heating and did not burn incense indoors.

Conclusion

This study reveals for the first time that exposure to multiple categories of PM_{2.5}-bound PAHs was associated with significant alterations of lipid profiles among a general community population in Beijing, suggesting that atmospheric PAH exposure might be a novel risk factor for changing of lipid profiles and even afterwards cardiovascular diseases. Among blood lipids, HDL-C and TG were significantly associated with multiple categories of PAHs. Among lipid indices, CRI-I, CRI-II and AC were significantly associated with multiple categories of PAHs. Our results also highlighted that even for the non-carcinogenic PAHs, their adverse effects on lipid metabolism and chronic diseases should not be overlooked. These findings are novel and of great significance to public health by addressing the knowledge gap between atmospheric PAHs exposure and lipid profiles disruption.

Abbreviations

CVDs

Cardiovascular diseases

PM_{2.5}

Particulate matter in aerodynamic diameter less than 2.5 µm

PAHs

Polycyclic aromatic hydrocarbons

OC

Organic carbon

EC

Element carbon

NAP

Naphthalene

ACY

Acenaphthylene

ACP

Acenaphthene

FLU

Fluorene

PHE

Phenanthrene

ANT

Anthracene

FLT

Fluoranthene

PYR

Pyrene

BaA

Benzo(a)anthracene

CHR

Chrysene

BbF

Benzo(b)fluoranthene

BkF

Benzo(k)fluoranthene

BaP

Benzo(a)pyrene

IcdP

Indeno(1,2,3-cd)pyrene

DahA
Dibenz(a,h)anthracene
BghiP
Benzo(g,h,i)perylene
LMW-PAHs
low-molecular-weight PAHs
HMW-PAHs
high-molecular-weight PAHs
c-PAHs
Carcinogenic PAHs
nc-PAHs
Non-carcinogenic PAHs
HDL-C
High-density lipoprotein cholesterol
LDL-C
Low-density lipoprotein cholesterol
TC
Total cholesterol
TG
Triglycerides
CRI
Castelli risk indexes
NHC
Non-HDL cholesterol
AC
Atherogenic coefficient

Declarations

Ethics approval and consent to participate

The ethics was approved by Institutional Review Board of Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences (IBMS, CAMS). Each participant completed a written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by the China Medical Board (grant numbers 15-230); the China Prospective cohort study of Air pollution and health effects in Typical areas (C-PAT) (grant numbers MEE-EH-20190802); the Chinese Academy of Medical Science Innovation Fund for Medical Sciences (grant numbers 2017-I2M-1-009).

Authors' contributions

XW cleaned the data, performed the data analysis and drafted the manuscript; AL, MZ, JX and YM helped the organization and completion of filed research work; QX designed the longitudinal study and helped revise the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

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Figures

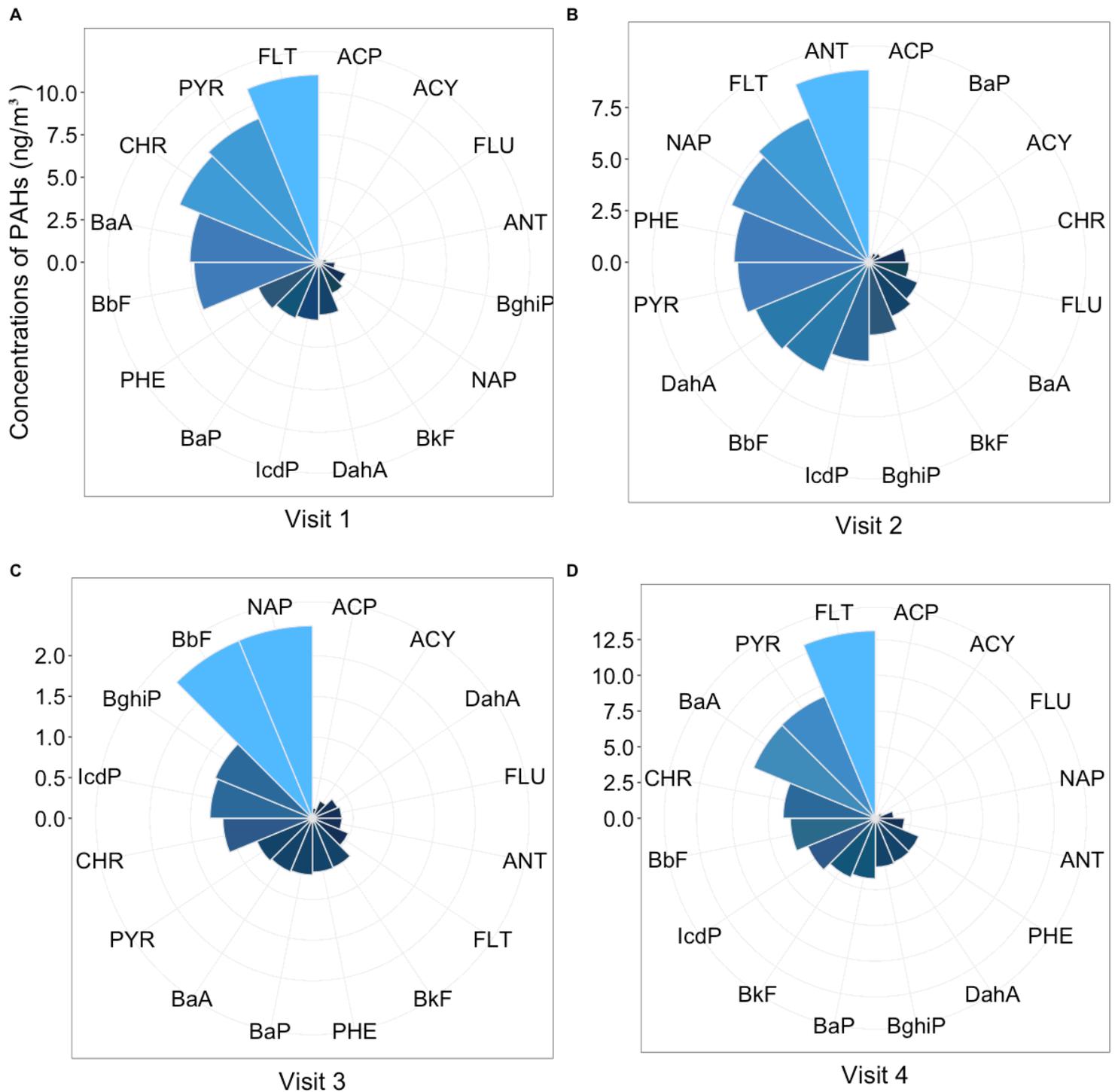


Figure 1

The concentrations of the original 16 priority PAHs (ng/m³) at each visit.

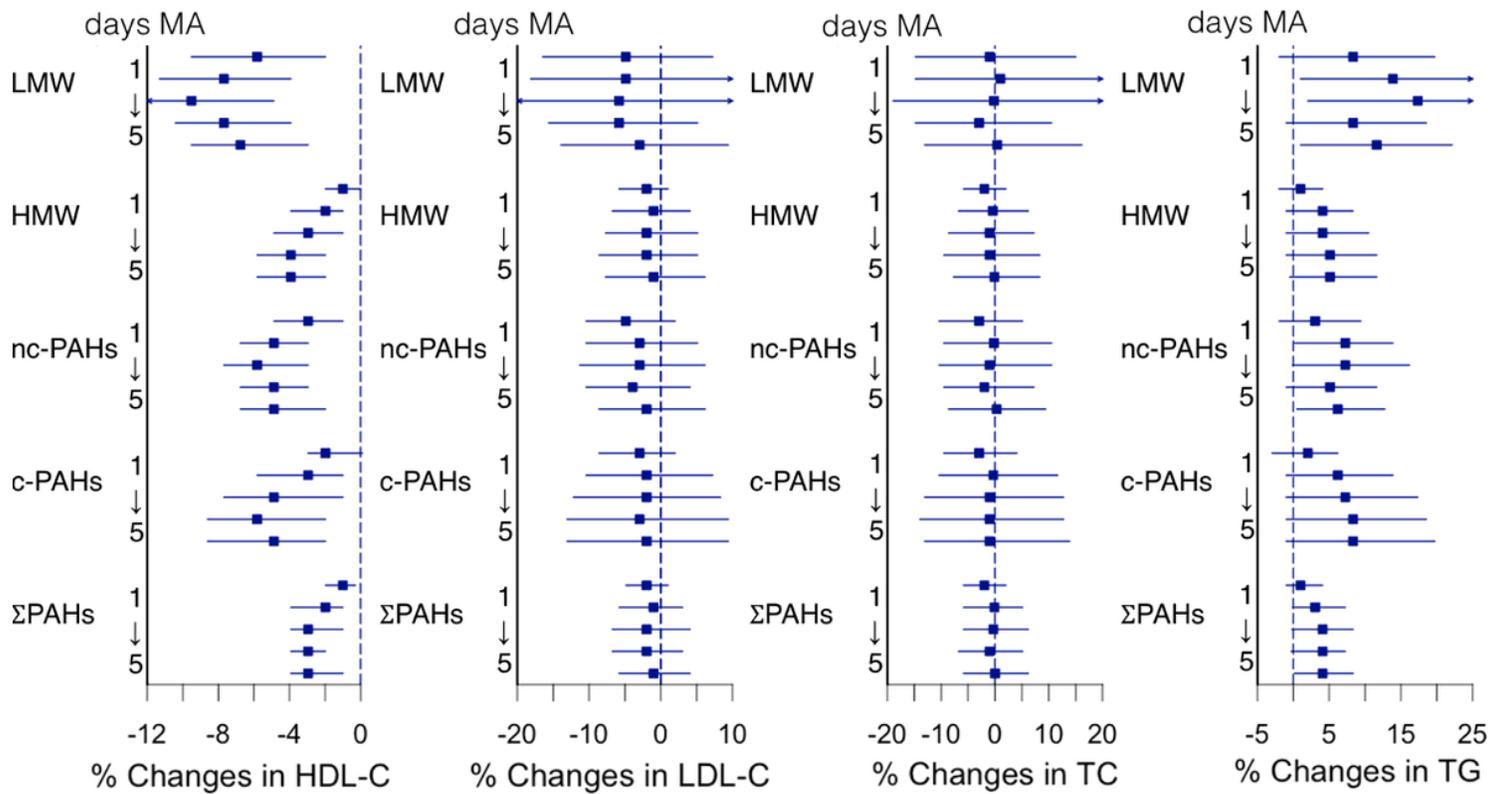


Figure 2

Changes in blood lipid associated with a 10 ng/m³ increase in different categories of PAHs.

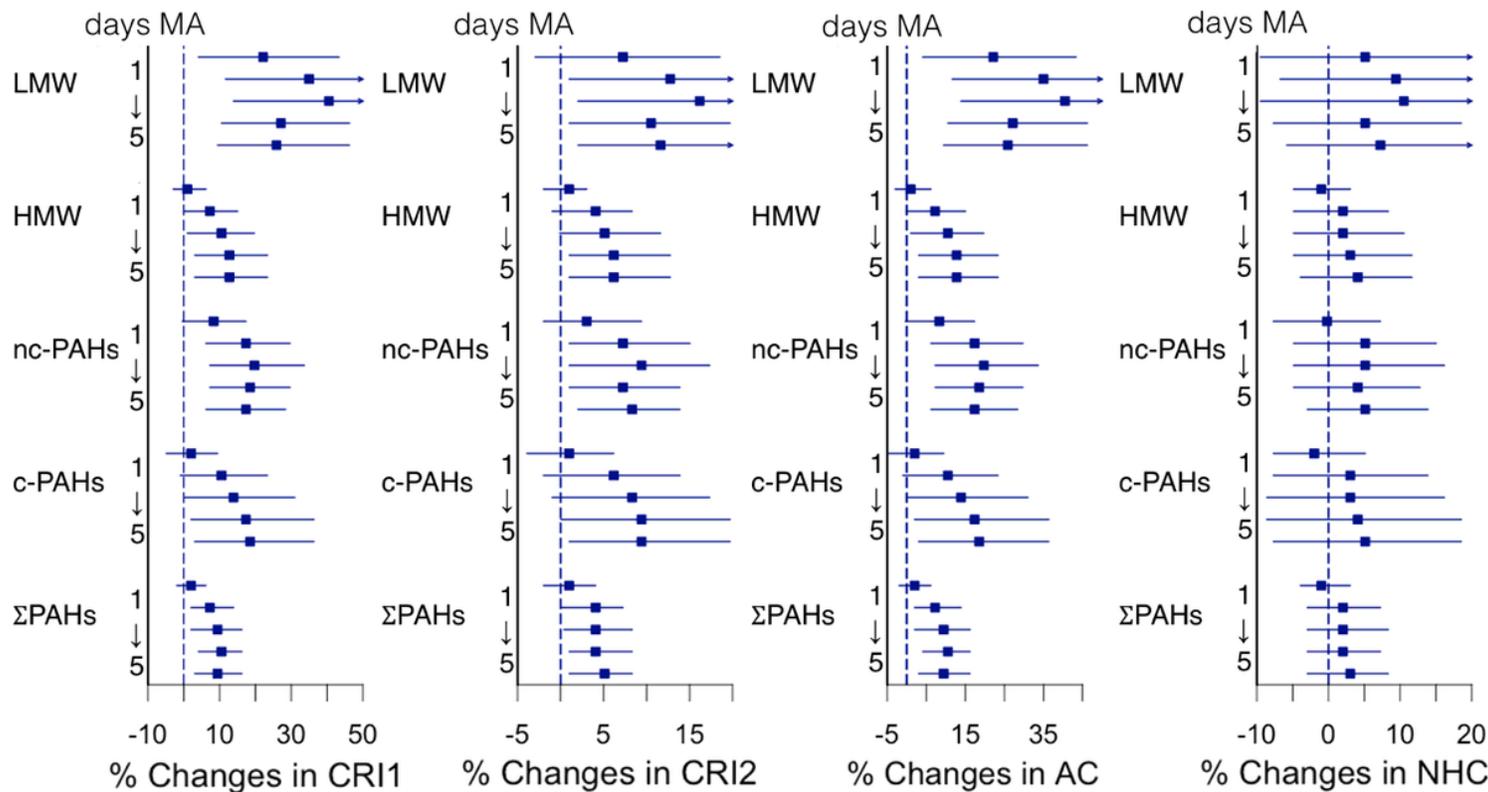


Figure 3

Changes in lipid indices associated with a 10 ng/m³ increase in different categories of PAHs.

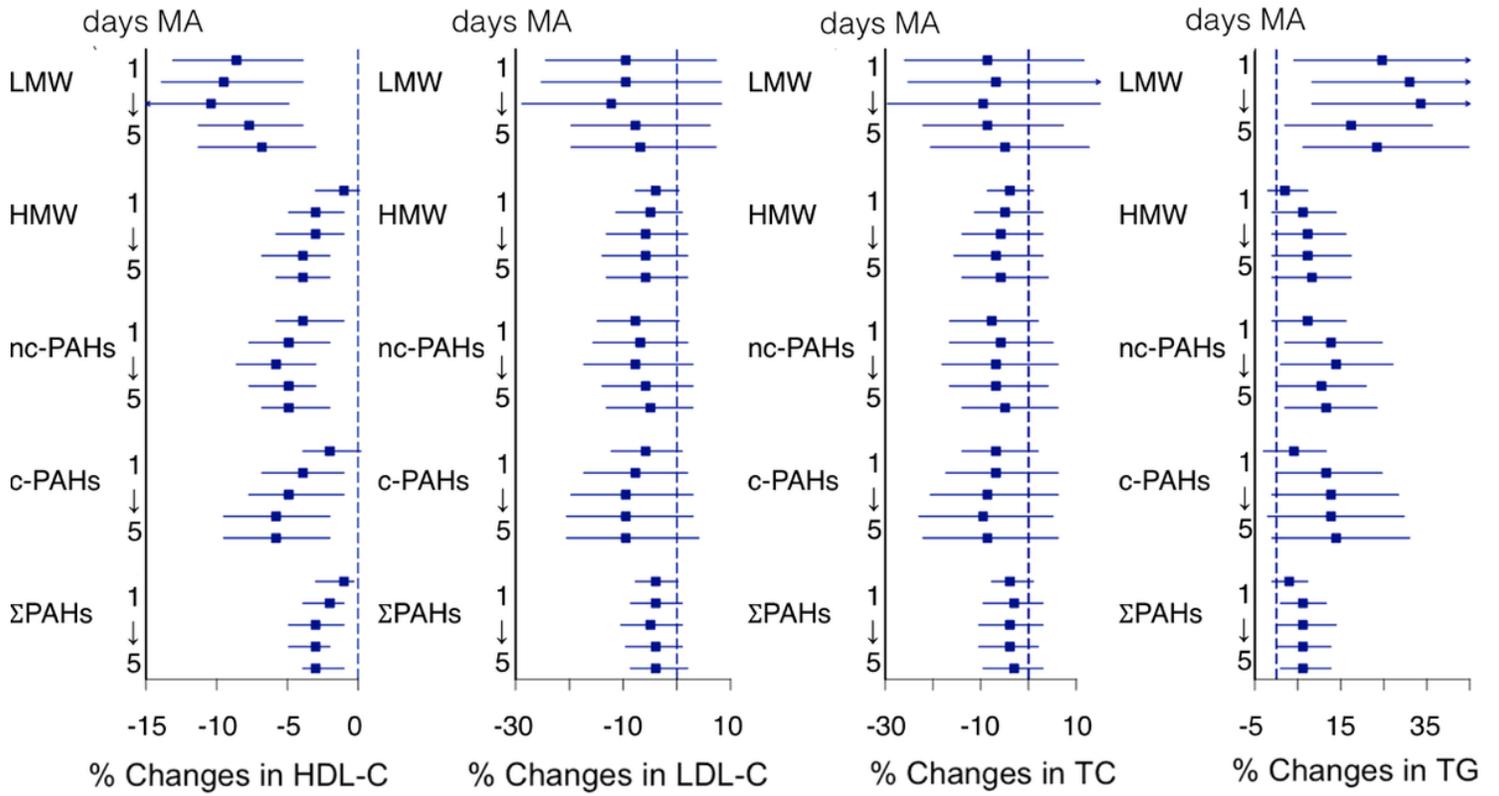


Figure 4

Changes in blood lipid associated with PAHs among participants from non-smoker residences.

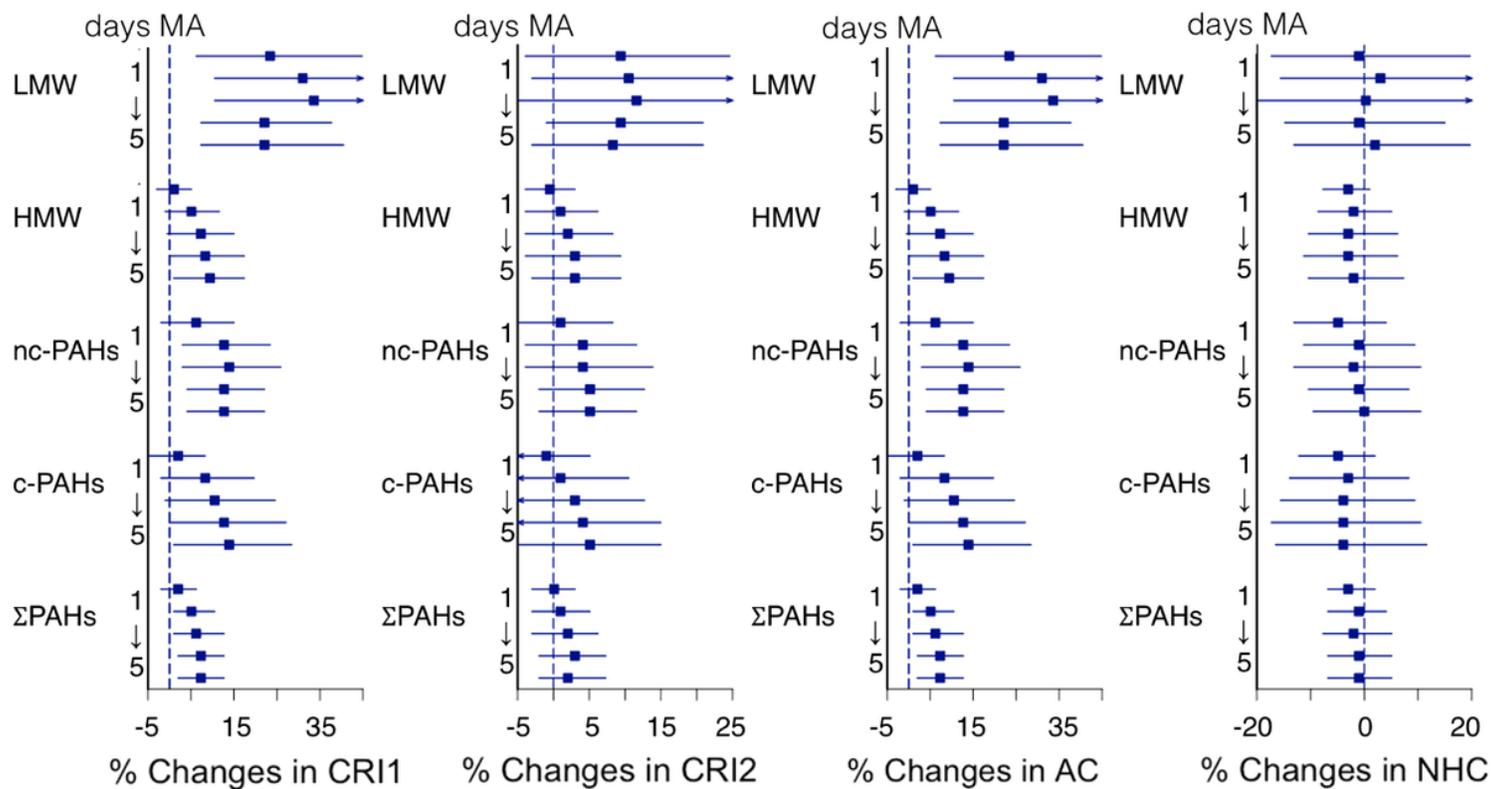


Figure 5

Changes in lipid indices associated with PAHs among participants from non-smoker residencies.

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